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Introduction: Astronauts continue to wear a compression garment during and immediately after landing to prevent orthostatic intolerance (OI). We recently developed a custom-fitted, 3-piece garment that consists of thigh-high stockings with biker-style shorts that provides continuous, gradient compression: 55 mmHg at the ankle that decreases to approximately 20 mmHg at the top of the leg and 15 mmHg over the abdomen. This garment has been shown to be effective in preventing symptoms of OI during a short stand test after Space Shuttle missions, but symptoms may persist for several days after a long-duration mission in some astronauts. The purpose of this study was to confirm the effectiveness of wearing these elastic, gradient compression garments during orthostatic testing after 2 weeks of 6° head-down tilt bed rest as a model of spaceflight and to determine whether they would impact recovery after bed rest. **Methods**: Eight (5 treatment, 3 control) of 16 subjects have completed this study to-date. All subjects wore the 3-piece garment from waking until tilt testing (~3 h) as a simulation of the timeline for astronauts on landing day (BR+0). Control subjects removed the garment after the tilt test. Treatment subjects wore the garment for the remainder of the day and wore lower compression thigh-high only garments on the day after bed rest (BR+1). Blood pressure, heart rate, and stroke volume responses to a 15-min 80° head-up tilt test were determined before 2 weeks of 6° head-down tilt, and on BR+0 and BR+1. Plasma volume (PV) was measured before each of these test sessions. Data are mean ± SE. Results: Compression garments prevented signs of OI on BR+0; all subjects in both groups completed the full 15-min test. Heart rate responses to tilt were lower on BR+0 than all other test days. Control subjects demonstrated a marginal PV decrease after bed rest, but showed typical recovery the day after bed rest (BR+0: 2.32 ± 0.15 L to BR+1: 2.79 ± 0.15 L). Treatment subjects did not recover PV the day after bed rest (BR+0: 2.61 \pm 0.23 L to BR+1: 2.61 \pm 0.23 L). **Conclusion**: Abdomen-high compression garments, which are effective in preventing post-bed rest orthostatic intolerance, may slow recovery of PV. Modified garments with reduced compression may be necessary to prevent prolonging recovery.